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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/576,097	05/22/2000	Laman Alani	6499.US.O2	3170

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EXAMINER
LUKTON, DAVID

ART UNIT	PAPER NUMBER
1653	8

DATE MAILED: 11/20/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/576,097	Alani
Examiner	**Art Unit**
David Lukton	1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Jul 2, 2001

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-19 is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-19 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

Applicants' election of Group 1 is acknowledged (claims 1-11, drawn to compositions in which the inhibitor is limited to G1). However, applicants did not elect a specie. Steven Crowley was informed of this, and on 11/6/01 he elected ritonavir. (The "elected specie" thus encompasses any of the claimed compositions that contain ritonavir). Affirmation of this election is required in response to this Office action.

Claims 1-11 are examined in part; claims 12-19 are also examined in this Office action.

*

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims recite the term "pharmaceutical composition", which implies an assertion of therapeutic efficacy. However, no such efficacy is in evidence. Certainly, there are numerous compounds known in the prior are which are not only effective to inhibit HIV protease, but which also inhibit HIV replication *in vitro*, and perhaps *in vivo* as well. One (or even all) of the compounds listed in claim 4 may be effective in this regard. But

inhibition of HIV replication, even *in vivo*, does not equate with therapeutic efficacy. Is is really the case that the compounds are effective to provide a perceptible improvement in the condition of a patient who is afflicted with AIDS, and is exhibiting clear signs of immunosuppression? This is the first question. The second issue is even more important than the first. The second issue pertains to the effects on bioavailability and pharmacokinetics of combining the HIV protease inhibitors with the fatty acid and propylene glycol (or ethanol). Applicants' position, no doubt, is that the compositions are novel, not because of the "active ingredients", but rather because of the change in bioavailability and pharmacokinetics afforded by the fatty acid and propylene glycol. Applicants have proposed an experiment (page 48, specification) which endeavors to assess the concentration of drug in serum subsequent to administration of the claimed composition. However, the route of administration (page 48, specification) is not specified, and no data is presented. Accordingly, no conclusion can be drawn. However, even if it turns out that the composition was administered orally, and even if it turns out that that the serum concentration was higher in the presence of a fatty acid and propylene glycol than is the case in their absence, this will not prove that the HIV protease inhibitors are therapeutically effective; more importantly, it will not constitute a demonstration that the the change in bioavailability and pharmacokinetics afforded by the fatty acid and propylene glycol is in a positive direction, i.e., that the therapeutic efficacy (if any) of the HIV protease inhibitors is at least as great in the presence of the fatty acid and propylene glycol as in their absence.

This ground of rejection can be overcome by deleting the word "pharmaceutical" from line 1 of claim 1.

*

Claims 3, 4, 8-10 , 14-18 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- In claim 3, line 2, the following designation appears: "2S, 3S, 5S)". There is an unmatched right-hand parenthesis here.
- In claims 4 and 10, the various abbreviations (e.g., VX 478, DMP 323, DMP 450, BMS 186318) may be used, but only if accompanied by the full name of the compound.
- In each of claims 4 and 10, the compound saquinavir is named. In each of these claims the words "isoquinol" and "ine" appear on separate lines, and no hyphen is present. However, this appears to be a typographical error.
- In claim 11, lines 4 and 5, there are at least two typographical errors.
- Each of claims 8, 9, 14, 15, 17, 18 recite weight percentages. However, there is no requirement or suggestion that the percentages must add up to 100%. For example, suppose that in claim 17, the two "active agents" together are present to the extent of 1%, the oleic acid is present to the extent of 15%, and the propylene glycol is present to the extent of 1%. What are the options for the remaining 83% of the composition? It is suggested that the cited claims be amended to require the percentages to add up to 100%.

*

The following is a quotation of the appropriate paragraphs of 35 U.S.C §102 that form the basis for the rejections under this section made in this action.

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2) and (4) of section 371(c) of this title before the invention thereof by the applicant for the patent.

*

Claims 1, 4-10 are rejected under 35 U.S.C. §102 (e) as being anticipated by Al Razzak (USP 5948436).

Al Razzak teaches the invention substantially as claimed. This includes (col 14 line 54+) the presence of water, at least when the composition is encapsulated

*

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1, 4-7, 9-10 are rejected under 35 U.S.C. §103 as being unpatentable over Sham (WO 97/21685).

Sham discloses (beginning on page 126, last paragraph) the invention substantially as claimed, except for the presence of water.

The instant claims impose no lower limit on the quantity of water, so, for example, 1 molecule of water per gram of composition would be encompassed. Also encompassed would be, e.g., water at the infinitesmal concentration of e.g., 0.00000000000001 parts per billion. Given the ubiquitous presence of water, and the hygroscopic nature of ethanol, one of ordinary skill would have expected water to be present at a level of at least 0.00000000000001 parts per billion.

Thus, the claims are rendered obvious.

*

Claim 1, 4-7, 9-10 are rejected under 35 U.S.C. §103 as being unpatentable over Sham (USP 5,914,332).

Sham dislcoses (col 74, line 1+) HIV protease inhibitors in combination with oleic acid and ethanol or proplyene glycol. The reference does not teach that water is present at a

level of 0.00000000000001 parts per billion. However, a chemist of ordinary skill would have recognized that it would be virtually impossible to exclude water at this level.

Thus, the claims are rendered obvious.

Applicants are advised that the specification will be amended to reflect the current states of cited applications as follows:

08/966495 → U.S.P. 6,232,333;

08/687774 → U.S.P. 6,037,157;

08/753201 → U.S.P. 5,914,332;

08/572226 → Abandoned

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton. Phone: (703) 308-3213.

An inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

DAVID LUKTON
PATENT EXAMINER
GROUP 1600